Exhibit M

Foreign Body Reaction to Meshes Used for the Repair of Abdominal Wall Hernias*

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ABSTRACT

Objective: To investigate the local tissue reactions to meshes that had been removed from humans.
Design: Open study
Setting: Surgical department of the technical University, Aachen, Germany.
Material: Samples of 17 non-absorbable meshes (1 polyester, 10 polypropylene, 2 reduced polypropylene, and 4 polytetrafluorethylene, PTFE) and 1 absorbable mesh (polyglactin 910) that had been implanted for repair of abdominal wall defects.
Interventions: Light and transmission electron microscopy, immunohistochemistry, and histological examination.
Main outcome measures: Signs of inflammatory response.
Results: Light microscopy showed chronic inflammatory tissue reaction, even after years, with pronounced differences among materials. Partial volume of inflammatory cells (%) varied from 32 in polypropylene, to 12 in expanded PTFE, 8 in polyester, and 7 in reduced polypropylene. Formation of connective tissue correlated significantly with the extent of the inflammatory reaction ($p < 0.01$). In meshes implanted for long periods there were still numerous macrophages at the interface between tissue and polypropylene (45%), polyester (45%), expanded PTFE (25%), and reduced polypropylene (22%). There was no difference in time dependent tissue reactions ($p = 0.19$).
Conclusion: Inflammation around alloplastic materials used to repair defects in the abdominal wall persists for many years. There was evidence of long term wound complications as a result of persistent foreign body reactions. Further studies are required to evaluate the long term tissue response to these materials.

Key words: surgical meshes, foreign body reaction, polypropylene, polyester, PTFE.

INTRODUCTION

The repair of an incisional hernia is a common problem, with recurrence rates of about 50% after simple closure by suture. Implantation of biomaterials has convincingly reduced the recurrence rate to less than 10% (32). Despite the broad acceptance of meshes in hernia surgery and their undoubted advantages in the clinical management of incisional or recurrent hernias, there is an increasing number of published reports describing local wound disturbances or other complications. In up to half, seromas are detectable by ultrasound, indicating local inflammation (32). The inflammatory reaction with its physiological wound contraction also causes the mesh to shrink and fold (1), its area is reduced to 60% of its origin size or even to 10% in the case of mesh plugs (1). Sharp edges may injure surrounding tissues, such as the spermatic cord (35). Implants have been found to have migrated to the bladder (15) and to the intestine (8). Coexisting fistula formation has always been a problem (10, 12, 17, 30, 34). Embedded in a wall of scar tissue, the alloplastic materials, particularly in large meshes, can cause appreciable limitation of the mobility of the abdominal wall with persistent complaints from patients (3, 17, 19, 26, 27, 38).

Laparoscopic techniques in hernia surgery with their associated implantation of alloplastic materials not only carry a risk of local wound complications, but mean that implantation is compulsory, although successful mesh-free methods (such as the Shouldice repair) are available. Because in some studies about 30% of the patients are younger than 40 years old, these aspects are even more important (11, 25).

In animal experimental studies mesh induces an initial inflammatory reaction which is regulated by the chemical nature of the implanted material, physical features such as the size of the surface in contact with the recipient tissue, and the mechanical characteristics of the implant (18, 23). In 1997 Amid indicated that different materials can have a profound influence on the clinical result (1). Interestingly, in most clinical studies in humans, these meshes are described as inert

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Table I. *Revision surgery after mesh implantation*

Case No.	Sex	Age (years)	Implanted mesh	Interval (months)	Revision surgery	Observations
1	M	63	Mersilene® as reinforcement of the visceral say	98	Enlargement of mesh with Marlex®	Lateral mesh edge folded and rolled
2	F	55	Marlex® behind rectus muscle	6	Additional Mersilene® behind rectus muscle	Laterally rolled
3	M	62	Marlex® behind rectus muscle	15	Mesh explantation in peritonitis	Small bowel erosion by mesh
4	M	57	Marlex® on rectus fascia	24	Mesh explantation in local peritonitis	Buttonhole hernia with bowel perforation at edge of mesh
5	F	49	Marlex®, as a temporary abdominal wall closure in peritonitis	7	Mesh explantation and primary closure of abdominal wall	Granulation tissue on the mesh
6	M	73	Marlex® on rectus fascia	5	Mesh explantation, Atrium® behind rectus muscle	Buttonhole hernia
7	M	44	Marlex® as Lichtenstein repair	14	Transinguinal preperitoneal prosthesis with Marlex®	Buttonhole hernia
8	M	64	Marlex® as transinguinal preperitoneal prosthesis	6	Mesh explantation for recurrent hernia, preperitoneal Atrium® mesh	Marlex® mesh shrunk and rolled, recurrent hernia at the edge.
9	M	28	Prolene® laparoscopic in primary inguinal hernia	19	Mesh removed because of pain after adhesiolysis at sigmoid area twice	Mesh shrunk and rigidly embedded in scar tissue.
10	F	55	Prolene® mesh on rectus fascia	2	Revision because of organised haematoma, Atrium® mesh behind rectus muscle	Mesh and haematoma in pseudocapsule.
11	F	59	Atrium® mesh	3	Implantation of a 2nd mesh for enlargement	Pseudorecurrence at the scar tissue
12	M	61	Vicryl® mesh	9	Shouldice repair	Scar tissue
13	M	60	Gore-Tex® on rectus fascia	97	Mesh explantation, repair by suture	Buttonhole hernia
14	M	56	Gore-Tex® laparoscopic preperitoneal	7	Mesh explantation, Shouldice repair	Mesh rolled, embedded in capsule, no junction through the pores
15	M	50	Gore Tex® on rectus fascia	60	Marlex® implantation behind rectus muscle	Buttonhole hernia
16	M	41	Gore-Tex® in between rectus fasciae	8	Implantation of Atrium® mesh behind rectus muscle after fifth recurrent incisional hernia	Mesh shrunk, embedded in capsule, no junction through the pores
17	F	67	Vypro®	3	Relaparotomy for reflux disease	Mesh well vascularised, no scar plate
18	M	61	Vypro®	12	Laparotomy for recurrent tumour	Good vascularisation, mesh just palpable

materials, but we know of no systematic morphological examinations of the long term effects of the meshes that are commonly used for hernia repair in humans.

Basic elements of our understanding of the local integration of mesh implants into the abdominal wall are mainly experimental studies in laboratory rodents. The aim of the present study was to investigate the local tissue reaction of mesh samples obtained from patients.

MATERIAL AND METHODS

Tissue samples: A total of 18 samples of implanted meshes were removed during revision operations and all samples were examined morphologically (Table I). Except for one Marlex® mesh with a fistula to the intestine, no mesh showed macroscopic signs of infection or inflammation.

Morphological study: Specimens were studied by light and transmission electron microscopy (TEM). For light microscopy, tissue samples were fixed in 10% formalin, embedded in paraffin, and sections stained with haematoxylin and eosin, periodic-acid Schiff (PAS) plus diastase, and elastic van Gieson (EvG). For TEM, tissue specimens were fixed in 3% cacodylate-buffered glutaraldehyde for 30 minutes. After

Table II. *Morphometry at the interface of implanted mesh materials*

Data are expressed as mean (SD) % except where otherwise stated.

	Polyester (Mersilene)	Polypropylene (Marlex, Prolene, Atrium)	ePTFE (Gore Tex)	Polypropylene and Polyglactin 910 (Vypro)	Polyglactin 910 (Vicryl)
Number	1	10	4	2	1
Age of patients	63	55 (12.3)	52 (8.3)	64 (4.2)	61
Implantation time (months)	98	11 (7)	43 (45)	8 (6)	9
Partial volume					
Inflammation	8	32 (12)	12 (4)	7 (1)	0
Connective tissue	27	39 (9)	28 (15)	17 (2)	89
Fat tissue	63	31 (13)	57 (17)	58 (3)	3
Vascular tissue	6	9 (2)	11 (4)	12 (2)	6
Cells at the interface					
Macrophages	45	45 (13)	25 (6)	22 (4)	0
PMN	11	13 (7)	1 (1)	1 (2)	0
Lymphocytes	7	6 (3)	2 (0)	4 (2)	0
Fibroblasts	19	20 (6)	12 (2)	10 (3)	11

fixation in osmium buffered in 0.1 M cacodylate they were dehydrated in ethanol and embedded in Epon. Semi-thin sections (1.0 μm) were stained with methylene blue-azure II. Ultra-thin sections were mounted on copper grids, stained with uranyl acetate and lead citrate, and examined with a transmission electron microscope (Philips, EM400T).

Immunohistochemistry: Light microscopy and TEM were controlled by immunohistochemical tests which were done on the material embedded in paraffin using the avidin-biotin complex method, with diaminobenzidine as a chromogen.

Antibodies: Antibodies included polyclonal rabbit anti-human CD3; 1/50 and monoclonal mouse anti-human CD68; 1/50 (DAKO, Hamburg, Germany) and monoclonal anti-human CD15; 1/10 (Becton Dickinson, Heidelberg, Germany)

Morphometry: The morphometric evaluation consisted of a quantitative cell analysis of the inflammatory reaction and the soft-tissue reaction. The cells were counted in each of five slides stained with haematoxylin and eosin in 10 fields at a grid of 10 points (×140, area 0.106 mm^2) and in the interface (0–300 μm, area 636 μm^2) at TEM. We measured the inflammatory infiltrate (partial volume (PV) %), connective tissue (PV %), fat cells (PV %), vessels (PV %), macrophages (%), leucocytes (%), and fibroblasts (%). To evaluate the shrinkage of the meshes (Marlex® and Soft hernia mesh®) we compared the width of the pores over a distance of 2 cm in 10 slices/probe with the textile structure.

Statistics: Statistical analysis is carried out using the Statistical Package for Social Sciences (SPSS 5.0.1) software. The significance of differences in the functional and morphological results were analysed using a corrected analysis of variance [LSD-test (Least-Significant-Differences) according to Bonferroni], followed by the independent t-test when a significant difference was found. The bivariate correlation between variables was described by the Pearson's correlation coefficient. Probabilities of less than 0.05 were accepted as significant.

RESULTS

General observations: Between 1994 and 1997 we acquired a total of 18 mesh samples from 13 male and five female patients (mean (SD) age of 56 (10) years). The implantation time varied from 2 to 98 months (mean (SD) 21 (30) months, median 8.5). The samples comprised one polyester mesh, 12 polypropylene meshes (seven Marlex®, two Prolene®, two Vypro®, one Atrium®), four polytetrafluorethylene (PTFE, Gore-Tex®) and one absorbable polyglactin 910 (Vicryl®) mesh.

Fourteen of the 18 patients required revision for recurrence of the hernia. One patient had a bowel perforation at the edge of the mesh and one an intestinal fistula. Two revisions were done for different diseases (Table 1). All the meshes removed seemed to be shrunk and deformed (Fig. 1).

In all materials, the quantity of inflammatory cells (macrophages and polymorphonuclear leucocytes) was significantly and directly correlated with the number of fibroblasts ($p < 0.01$). The amount of fat tissue was inversely proportional to the amount of connective tissue ($p < 0.01$) and decreased over time ($p < 0.05$). No other variable correlated significantly with the duration of implantation (Pearson's correlation coefficient $r = -0.31$, $p = 0.19$).

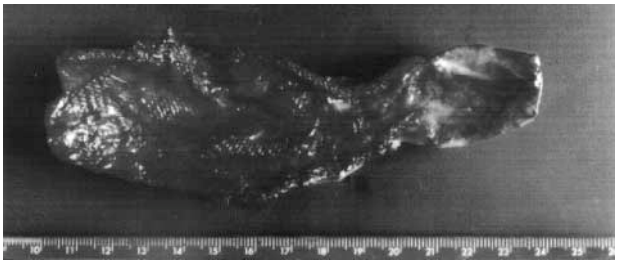

Fig. 1. Marlex® mesh six months after transinguinal and preperitoneal implantation; the prosthesis has shrunk and the free edges look rolled.

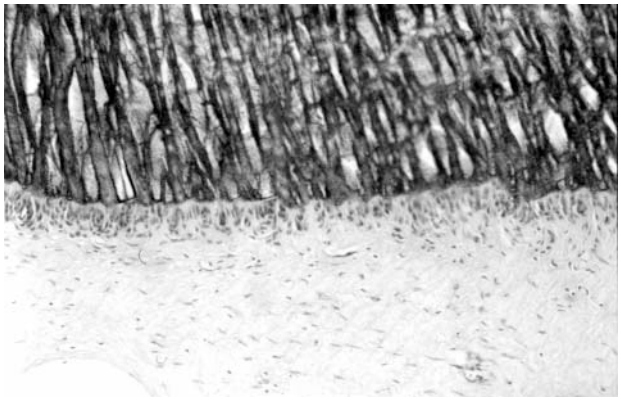

Fig. 2. No penetrating tissue reaction to PTFE mesh 60 months after implantation as on-lay on the external fascia; haematoxylin and eosin, original magnification ×250.

Expanded polytetrafluorethylene (ePTFE; Gore-Tex®): The interface reaction of the four ePTFE meshes (implantation time 7–97 months) was characterised by inflammation dominated by macrophages. Light microscopy showed only poor integration of ePTFE meshes into the abdominal wall (Fig. 2). The implant was mainly surrounded by connective tissue while penetration of cells into ePTFE pores or adherence to the surface were rare. TEM of the extracellular matrix showed that newly-formed collagen bundles were more tangled up than orientated in parallel lines with little cross-linking.

The morphometrically calculated partial volume of connective tissue varied between 10% and 46%, and the quantity of fat tissue between 71% and 33%. PMN were found only exceptionally, but macrophages, epithelioid cells, multinucleated foreign-body giant cells, and fibroblasts were still detectable after eight years. The vascularisation of the mesh-fibre/connective tissue interface was comparably high with a partial volume of 11%, whereas the total partial volume of all inflammatory cells was relatively low at 12%.

Polyester (Mersilene®): The single polyester mesh showed mainly chronic local inflammation characterised by the formation of typical foreign body granulomas and numerous multinucleated giant cells. Histological signs of an acute inflammation such as CD15-positive PMN or necrosis could be detected only in small areas or around single mesh filaments. Collagen synthesis was low compared with polypropylene, forming a thin capsule around the mesh fibres, in which there were occasional small aggregates of CD3-positive T-lymphocytes.

Overall, the partial volume of all inflammatory cells was reduced compared with both polypropylene and ePTFE meshes. Pores were filled with mainly fat tissue and only a few pores showed penetrating connective tissue. The partial volume of vessels was low at 6%. Despite the relatively long implantation duration of 98 months, there was a persistent localised inflammatory reaction together with incomplete integration of the mesh into the abdominal wall.

In accordance to the assumed slow but obligant degradation (31) we find signs of mechanical fragmentation in this sample.

Polypropylene (7 Marlex®, 2 Prolene®, 1 Atrium®): All the polypropylene meshes (implantation time 3–24 months) had similar histological patterns after explantation.

Commonly, there was a predominant foreign body reaction with typical foreign body granulomas including epithelioid cells and giant cells. However, and contrary to ePTFE, polyester, and the reduced polypropylene mesh there was persistent acute inflammation with varying amounts of CD15-positive PMN and focal fibrinoid necrosis in most cases. The inflammatory process was accompanied by pronounced perifilamentous fibrosis with an extensive amount of deposited collagen fibres (Fig. 3). Adjacent to the mesh the fibres were mainly orientated parallel to the polypropylene threads. In the periphery, connective tissue with numerous collagen fibres formed a thick capsule in which the whole mesh was integrated. These mesh modifications were characterised by complete penetration of connective tissue into the pores. The meshes and the newly formed connective tissues around the meshes formed a complex unit as a result. Fibroblasts were still common at the interface, whereas vascular structures were rare. After more than a year the inflammatory reaction was reduced but still detectable within the interface.

Compared with ePTFE and polyester, polypropylene had the most inflammatory and connective tissue cells in the interface, but least fat tissue and vascularisation. At 20%, polypropylene meshes had the most fibroblasts.

The mean (SD) pore width of these meshes had

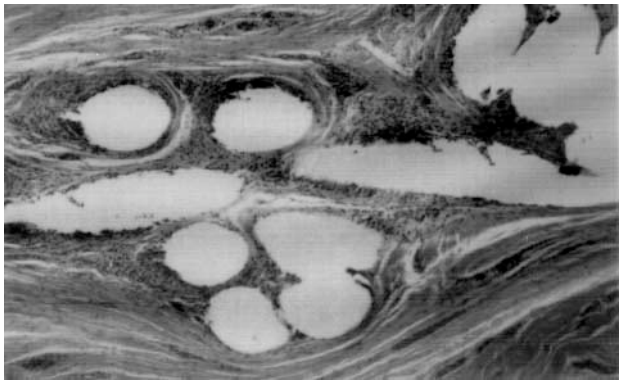

Fig. 3. Marlex® mesh 14 months after transinguinal preperitoneal prosthesis with marked fibrosis around the implant. Haematoxylin and eosin; original magnification ×100.

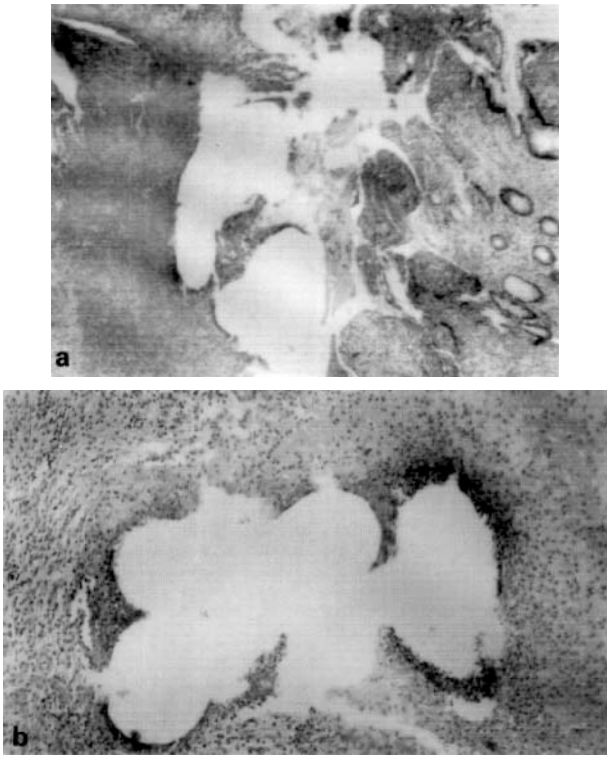

Fig. 4. Acute inflammation at the interface of the Marlex® mesh (a) with penetration into the intestine after 24 months (b); haematoxylin and eosin, original magnification ×250.

decreased considerably from 2.5 (0.5) mm initially to 2.1 (0.2) mm ($p < 0.05$, t-test). This corresponds to a reduced length of 17% or a reduced area of 31%, respectively.

One mesh had penetrated into intestine after 24 months. The tissue reaction was characterised by an acute, suppurating type of inflammation with extensive fibroid necrosis around the mesh fibres (Fig. 4).

Reduced polypropylene combined with polyglactin 910 (Vypro®): The inflammatory response of this mesh (implantation time 3 and 12 months, respectively) with a reduction of polypropylene to less than 30% of Marlex® is considerably reduced compared with the other polypropylene meshes (Marlex®, Prolene®). The tissue reaction was characterised by the formation of the foreign body granulomas with a moderate number of multinuclear giant cells. Signs of acute inflammation such as infiltrates of PMN and fibroid necrosis were rare. The collagen fibres formed moderate capsules that were centrally and concentrically orientated around single mesh filaments, whereas in the periphery there was a thin scar plate orientated parallel to the mesh (Fig. 6). The number of fibroblasts was low, in contrast to the pronounced vascularisation.

The mean (SD) pore width of this mesh had decreased considerably from 5.0 (0.6) mm initially to 4.0 (0.3) mm ($p < 0.05$, *t*-test). This corresponds to a reduction of 21% in length and of 38% in area, respectively.

Polyglactin 910 (Vicryl®): Nine months after implantation, this absorbable mesh had disappeared completely. The histological picture was that of a mature scar without any inflammation, a lot of connective tissue (89%), and small amounts of fat tissue (3%). Vascularisation was moderate with a partial volume of 6%. There were no signs of macrophages and PMN. Fibroblasts made up 11%, indicating little activity for remodelling of the scar tissue.

DISCUSSION

All patients in this retrospective study had had the typical complications of mesh implantation such as recurrent hernias after implantation in the onlay technique (buttonhole), bowel erosion by direct contact with sharp edged mesh, folding of the mesh as a consequence of shrinkage, and insufficient mechanical sealing by ePTFE after inappropriate integration of this special mesh into the abdominal wall.

Generally, reinforcement of the abdominal wall with biomaterials works by both direct mechanical sealing (sublay) and induction of a scar plate formation (polypropylene, polyester) (22). Mechanical properties of the artificial abdominal wall are in this case mainly regulated by the implantation techniques and the local fibrous tissue response induced by the chemical and physical properties of the implanted mesh (23).

Experimentally, all meshes cause an initial and chronic inflammatory tissue response in the recipient after implantation. The quantity and quality of the local inflammation depends directly on the mesh concerned. This induces and controls the connective tissue

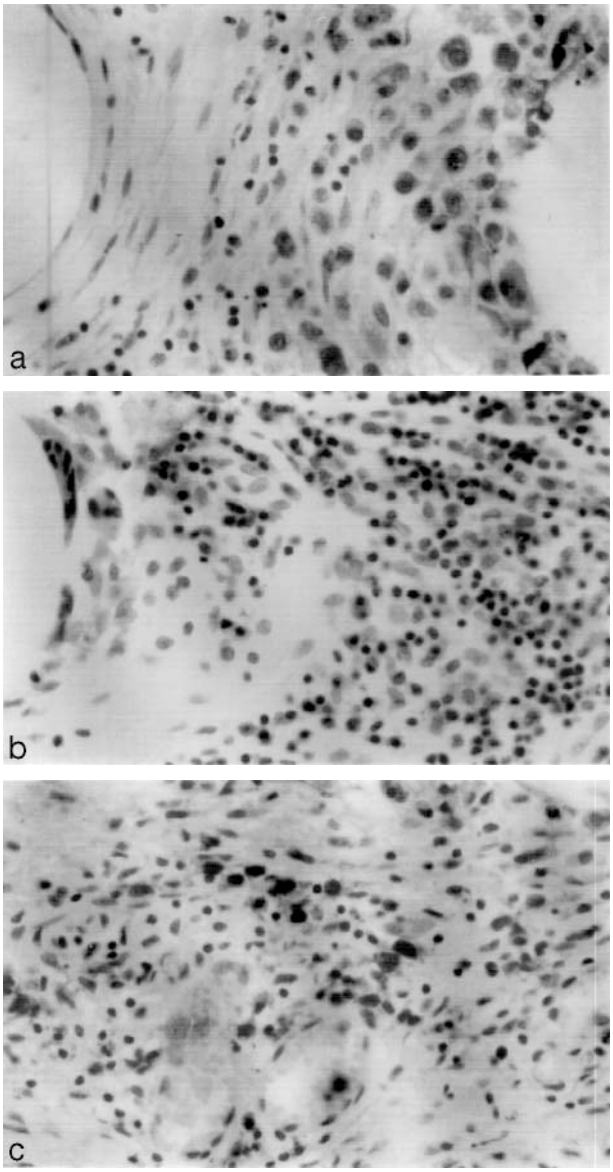

Fig. 5. Immunohistochemical differentiation of inflammatory cells. The example shows a Prolene® mesh 19 months after transabdominal preperitoneal prosthesis: (a) CD3-positive T-lymphocytes, (b) CD68-positive macrophages and giant cells and (c) CD15-positive PMN; original magnification ×400.

response. Although in the present study only a few samples of mesh were examined, a specific, material-related tissue was shown histologically and confirms the persistence of inflammation for years. Though the detectable inflammation might be influenced by the presence of recurrent hernia or fistula formation, the data always show a persistent foreign body reaction that is independent of the implantation time, but considerably affected by the type of mesh material. There is no significant correlation between implantation time and inflammation which may be interpreted as a missing development in the biological tolerance to the meshes. As with the animal experiments, the histological appearance remains constant after three months. This confirms the results of Dayer et al., who saw identical tissue reactions after one year (7).

Formation of connective tissue correlates significantly with the amount of inflammation, but the partial volume of connective tissue allows no prediction to be made about mechanical stability. Although clinical and experimental studies have proved that the implantation of the absorbable polyglactin 910 leads to collagen-rich scar tissue, hernia repair with this mesh is nearly always followed by recurrent hernia (13, 37). In contrast, modifications of polyester and polypropylene mesh achieve sufficient closure of the hernia with low recurrence rates, though the relative amount of connective tissue is low compared with polyglactin 910.

In accordance with the published data, ePTFE induces only a scanty inflammatory reaction and a capsule of connective tissue without interlinking bridges through the mesh, while polyester and polypropylene lead to a pronounced chronic inflammation (2, 3, 9) and a strong interlinking formation of connective tissue through the mesh-pores. This embedding connective tissue forms a rigid scar plate and is responsible for mesh shrinkage of 20% in length or 40% in mesh area, respectively, compared with the original mesh in its native, non-implanted condition. These findings fully confirm the report of Amid (1) and the experimental results in dogs (21).

The tissue reaction at the interfaces between ePTFE, polypropylene and polyester is similar to the findings in animal experiments and characterised by many macrophages, granulomas, and foreign body giant cells (4, 5, 17, 24, 30, 34). A reduced amount of polypropylene, larger pores and the addition of absorbable polyglactin 910, covering the polypropylene surface, prevents massive inflammation, as was recently shown in rodents (23).

The polyester induced tissue reaction shows comparatively little inflammation but mainly granulomas with lots of macrophages, whereas polypropylene shows an increased amount of inflammation and connective tissue. The dense assembly of macrophages and fibroblasts indicates persistent remodelling of the scar tissue. The Vypro® with the reduced amount of polypropylene (20) showed a pronounced reduction in inflammation, and improved integration into surrounding tissue. Similar differences in foreign body reactions depending on the implanted material were reported by Beets et al. who found reduced inflammation with a monofilament polypropylene mesh compared with a multifilament polypropylene mesh (2).

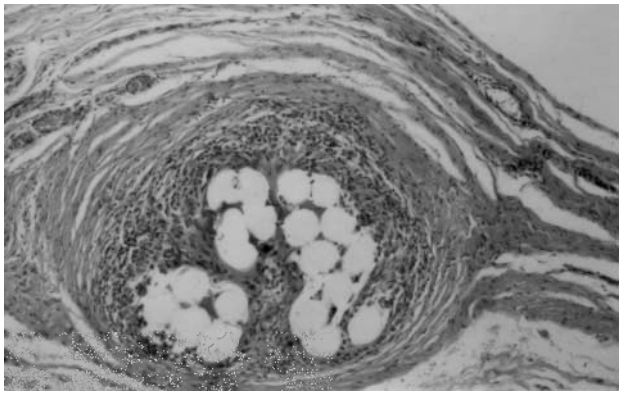

Fig. 6. Vypro® mesh three months after implantation showing a moderate fibrosis and inflammation, haematoxylin and eosin, original magnification ×1000.

Altogether, these data show that all meshes cause a persistent inflammatory reaction at the interface between polymer-fibres and recipient tissues even if the meshes have been implanted for months or years. The adaptability of the host and the inertness of the meshes are obviously limited, resulting finally in a separation of the mesh by a foreign body granuloma with a surrounding collagen capsule to protect the entrapping host tissues.

Despite many reports of revision operations after mesh implantation, systematic examinations of the foreign body reaction have not been made. Although we could find no histological data after long term implantation of commercially-available modified meshes, the inertness of these applications in humans is generally accepted. The basis for this statement are usually animal experiments with an implantation time of 3 to 6 months, and clinical studies with a follow-up of one to 10 years mainly in cases of recurrences.

In the 1960s and 70s, animal experimental studies proved that sarcomas could be induced by alloplastic materials in mice and rats (6, 29). The development of lymphomas by polyester meshes in dogs (14) and the clinical observations of at least fifteen published Dacron-induced sarcomas (16, 28, 31, 36, 39, 40) underline the fact that systematic studies are essential to throw more light on the long term effects of the implantation of alloplastic meshes in humans. These would help to exclude any real long term risks. Fortunately, up to now mesh-related sarcomas have not been seen and the number of complications is still rare. Nevertheless, the persistence of a foreign body reaction at the mesh-tissue interface might cause severe problems, particularly in the young patients, in whom the mesh is expected to hold for several decades.

Because of the uncertainty of the long term biocompatibility, the use of non-absorbable meshes in primary hernias should therefore be reconsidered if these patients can be successfully treated by conventional suture techniques with good results (33).

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RÉSUMÉ:

But: Étudier les réactions tissulaires locales par rapport aux filets retirés du corps humain.
Type d'étude: Étude ouverte.
Provenance: Département de chirurgie, hôpital universitaire, Aachen, Allemagne.
Sujets: Des échantillons de 17 filets non résorbables (1 en polyester, 10 en polypropylène, 2 en polypropylène comprimé et 4 en polytétrafluoréthylène PTFE) et un filet résorbable (polyglactine 910) qui avaient été posés dans le cadre d'une réfection de paroi abdominale défectueuse.
Intervention: Microscopie normale et électronique, chimie immuno-histologique, examen histologique.
Principaux critères de jugement: Les signes de la réponse inflammatoire.
Résultats: La microscopie normale démontra une réaction tissulaire de type inflammation chronique, même après des années, avec des résultats variant d'une manière importante selon le matériel. Le volume partiel des cellules inflammatoires (%) variait de 32 lymphocytes pour le polypropylène, à 12 dans les cas de PTFE expansé, 8 pour le polyester, et 7 pour le polypropylène renforcé. La formation de tissus conjonctif était en étroite corrélation avec l'importance de la réaction inflammatoire ($p < 0.01$). Dans les filets implantés depuis une longue période, il y avait encore de nombreux macrophages au niveau de l'interface entre les tissus et le polypropylène (45%), polyester (45%), le PTFE expansé (25%) et le polypropylène renforcé (22%). Il n'y avait aucune différence en ce qui concerne les réactions tissulaires dépendantes du temps ($p = 0.19$).
Conclusions: Les réactions inflammatoires autour des matériaux de type alloplastic utilisés pour réparer les déficits de la paroi abdominale persistent pendant des années. Nous n'avons constaté aucune complication de cicatrice, à long terme, comme résultat de la réaction inflammatoire envers les tissus étrangers persistants. Nous pensons que des études complémentaire sont nécessaires pour évaluer la réponse à long terme à ce type de matériau.

Mots-clés: Filets chirurgicaux, réaction contre des corps étrangers; polypropylène; polyester; PTFE.

ZUSAMMENFASSUNG

Aufgabenstellung: Untersuchung über die Gewebsreaktionen, an der Grensfläche zu implantierten chirurgischen Meshes.
Vorhaben: Offene Studie.
Einrichtung: Universitätsklinikum, Deutschland.
Gegenstand: Proben von 17 nicht-resorbierbaren Meshes (1× Polyester, 10× Polypropylen, 2× reduziertes Polypropylen, 4× Polytetrafluorethylen, PTFE) und 1 resorbierbares Mesh (Polyglatin 910), welche zum Verschluß von Bauchwanddefekten implantiert wurden.
Eingriffe: Licht- und Transmissions-Elektronenmikroskopie, Immunhistochemie und histologische Untersuchung.
Meßergebnisse: Anzeichen von entzündlichen Veränderungen.
Ergebnisse: Unter dem Lichtmikroskop zeigten sich, auch nach Jahren, chronisch entzündliche Gewebsreaktionen, mit deutlichen material-abhängigen Unterschieden. Der Volumenanteil der Entzündungszellen schwankt zwischen 32% bei Polypropylen, 12% bei PTFE, 8% bei Polyester und 7% bei dem reduziertem Polypropylen-Mesh. Das Ausmaß des induzierten Bindegewebes korreliert signifikant mit dem Ausmaß der Entzündungsreaktion ($p < 0.01$). Bei chirurgischen Meshes, die für längere Zeit implantiert waren, wurden zahlreiche Makrophagen an der Grenzfläche zum Implantat gefunden mit einem Anteil von 45% bei Polypropylen, 45% bei Polyester, 25% bei PTFE und 22% bei dem reduzierten Polypropylen-Mesh, ohne signifikante Beeinflussung durch die Implantationszeit ($p = 0.19$).
Schlußfolgerung: An der Grenzfläche zu Meshes, die zum Verschluß von Bauchwanddefekten eingesetzt wurden, läß sich auch nach mehreren Jahren eine persistierende inflammatorische Gewebsreaktion nachweisen mit entsprechenden Langzeit-Komplikationen als Folge der chronischen Fremdkörperreaktion. Weitere Studien sind zur Erfassung der Langzeit-Gewebsreaktion auf diese Materialien erforderlich.

РЕЗГОМÉ

Цель: Изучить локальную тканевую реакцию на сетчатый протез, который был удален у пациентов.
Характер исследования: Открытое исследование.
Клиника: Учебный госпиталь, Германия.
Материал: Образцы 17 нерассасывающихся сетей (1 полиэстеровая, 10 полипропиленовых, 2 редуцированных полипропилена, 4 политетрафлюроэтиленовых) и 1 резорбируемая сеть (полиглактин 910), которые были инплантированы при лечении грыж передней брюшной стенки.
Методы: Световая и трансмисионная электронная микроскопия, иммуногистохимия и гистологическое исследование.
Задачи исследования: Признаки инфламматорной реакции.
Результаты: Световая микроскопия показала хроническую воспалительную тканевую реакцию даже спустя годы различной степени выраженности в зависимости от материала. Парциальный объем воспалительных клеток (в %) варьировался от 32 в полипропилене до 12 в ПТФЭ, 8 в полиэстере и 7 в редуцированном полипропилене. Формирование соединительных тканей коррелировалось статистически достоверно с выраженностью воспалительной реакции ($p < 0.01$). В имплантированных сетках в течение длительного периода все еще можно было найти макрофаги в промежутках между ячейками: 45% в полипропилене, 45% в полиэстере, 25% в ПТФЭ и 22% в редуцированном полипропилене.
Выводы: Воспалительная реакция вокруг алопластических материалов, используемых для пластики передней брюшной стенки при грыжах, сохраняется в течение многих лет. Имеют место доказательства поздних осложнений со стороны операционной раны как результат персистирующей реакции на чужеродное тело. Было целесообразно провести дальнейшее исследование с целью изучения долговременного тканевого ответа на имплантацию чужеродных материалов.

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